FMD vaccine efficacy : attributes of higher potency vaccines and more recent findings

GFRA Meeting

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Control of FMD by Vaccination

Depends on the epidemiological situation and disease control policy of country.

For EU Countries, FMD is exotic and incursion more often than not results in a non-vaccination, stamping out measures

However, vaccination has been used in emergency situations and many countries rely on National or International Strategic FMD vaccine/antigen reserves

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Strategic Antigen Reserve

- Concentrated inactivated antigen held over liquid N_2
- Can be formulated to choice of adjuvant
- Potency (PD_{50}) 6 or more (for rapid protection and greater cross-reactivity)
- 500,000 doses can be ready within 4 days

- Some vaccine strains have held or hold a EU-compliant marketing authorisation
- Negotiations in progress for a ‘virtual, global antigen bank network’

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European Pharmacopoeia
FMD potency method

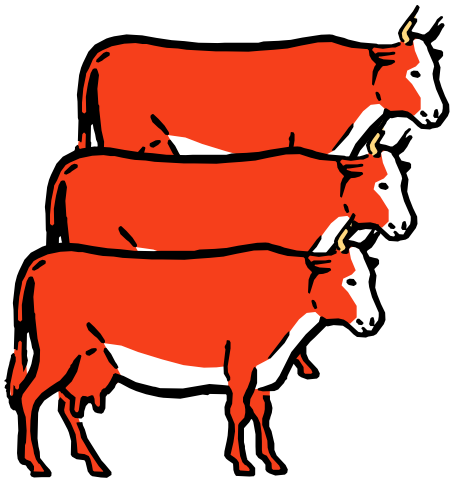
QUANTITATIVE

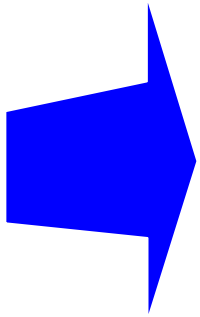
FMD Virus Challenge

21days post.vacc

PROTECTED

(absence of clinical signs on feet)





50% protective dose

3 groups of 5 cattle

each group vaccinated with a specific dose volume e.g. 1/1,1/4,1/16

3 PD_{50} minimum requirement

6 PD_{50} or more for strategic reserves

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European Pharmacopoeia
FMD potency method

Reducing animal experimentation in foot-and-mouth disease vaccine potency tests

Richard Reeve, Sarah Cox, Eliana Smitsaart, Claudia Perez Beascoechea, Bernd Haas, Eduardo Maradei, Daniel T. Haydon, Paul Barnett

Vaccine, Volume 29, 33, 26 July 2011, Pages 5467-5473,

Statistics associated with the current EP PD_{50} test (logistic regression or probit analysis) are inappropriate

That the OIE test statistics (Spearman–Kärber) is much better since it assumes the correct dose–response relationship

Identified a considerably better live animal challenge test approach –
two groups of 7 animals, one inoculated with a third of a dose of vaccine, and the other with a sixth of a dose –
for determining whether the PD50 is above 3 or 6, and is comparable to the OIE tests at determining both PD_{50} and % PPG.

This test could also provide further savings in live animal usage in exchange for small reductions in sensitivity and specificity.

Ideally we need to go over to a serological based approach.

Some key findings with higher potency FMD vaccines

1. Rate of protection against clinical signs following aerosol challenge in three main targets - within 4 days

2. Interval between vaccination and challenge as well as antigen payload/potency important to inhibiting local virus replication

3. Duration of immunity and protection following single immunisation - 6 months in sheep and cattle and at least 7 months in pigs

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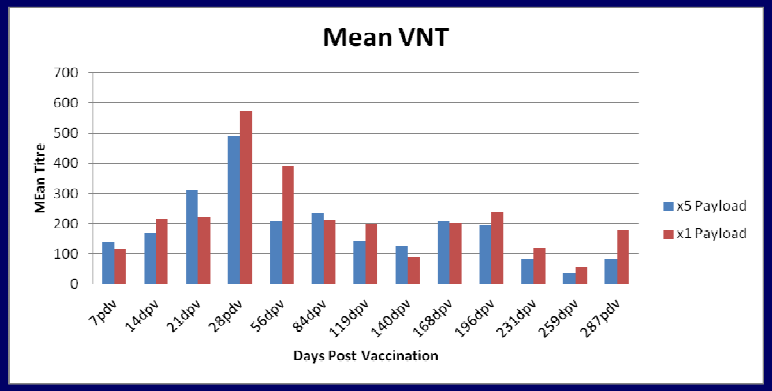
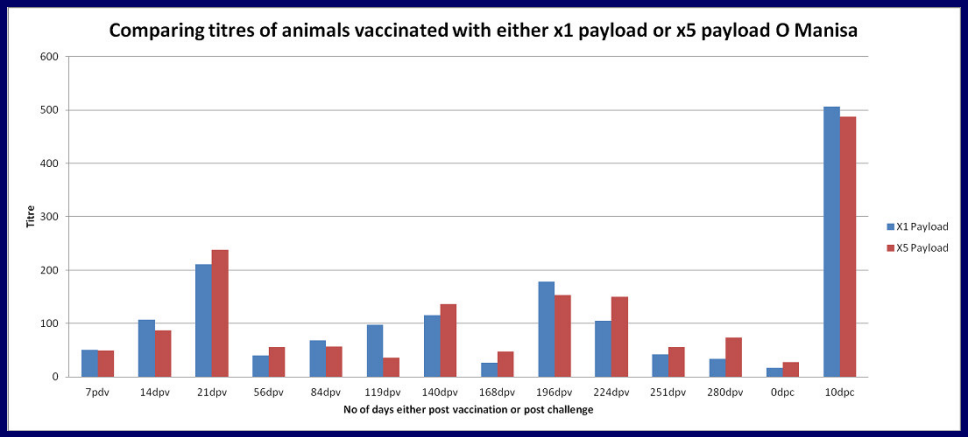
Further vaccine longevity trials in Cattle using ≥6PD$_{50}$ FMD vaccines

Asia1 Shamir



O1 Manisa



- Computational model and serology indicates protection at 6 months and a boost unnecessary.
- Not all cattle protected at 10 months post vaccination (11/19) - boost may be necessary prior to this time point.
- No increased benefit of 5 x fold Ag payload in terms of antibody responses or numbers protected.

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Some key findings with higher potency FMD vaccines

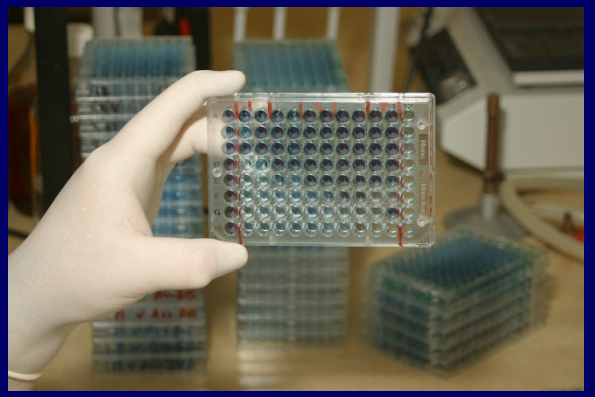
4. Can protect against serologically unrelated heterologous strains

- A serotype (Brehm et al 2008)
- O serotype (Nagendrakumar et al 2011)
- Asia1 serotype (Shamir vs Turkey 49/11 -*Yanmin Li*)

Higher potency vaccines that protect against serologically unrelated strains

Questions

the whole serological approach used



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Portfolio of vaccine strains required in a ‘bank’

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Efficacy against transmission

Quantified FMDV transmission parameter β from published experimental data to assess the effect of vaccination

From	To	GLM β per hour
Non-vac and Vac sheep	Non-vac sheep	0.0066
Non-vac and Vac sheep	Vac sheep	0.0011
Non-vac pigs	Non-vac sheep	2.4
Non-vac pigs	Vac sheep	2.056(0dpi) 0.692(-7dpi) 0.233 (-14dpi)
Non-vac cattle	Vac cattle	0.11
Non-vac pigs	Vac cattle	13.78
Non-vac pigs	Vac pigs	27.98 (0dpi) 2.18 (-7dpi) 0.17 (-14dpi)

•Sheep to sheep transmission LOW regardless of vaccination

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Some areas for the future in terms of evaluating and improving vaccine efficacy

Gaps in β parameter estimates

From:		To: non-vaccinated			vaccinated		
		Sheep	Cattle	Pigs	Sheep	Cattle	Pigs
non-vaccinated	Sheep	x			x#		
	Cattle		x[a]			x#	
	Pigs	x	x[a]	x[a]	x*	x#	x#
vaccinated	Sheep	x			x#		
	Cattle					x*	
	Pigs						

no available data in used experiments

x: transmission events available in used experiments

[a] scarce data, therefore beta could not be determined

* time-effect of vaccination could be demonstrated (2nd analysis)

time-effect of vaccination could not be demonstrated (2nd analysis)

Focus on inoculation approach – intradermal appears to provide scope for using much less antigen in pigs and cattle for protective immunity.